

***Amendments to the Claims***

*The listing of claims will replace all prior versions, and listings of claims in the application.*

1-60. (cancelled)

61. (currently amended) A high throughput parallel screening method of determining the pharmacological effect of a substance on the activities of different biological target molecules contained in test cells of the same type, comprising:

- (a) applying a defined amount of a test substance in one operation to more than one cellular substrates comprising test cells of the same type which differ in that they contain different biological target molecules;
- (b) measuring the effect of the substance on the biological activities of said different target molecules using a detection system using different assays or assay formats for each substrate; and
- (c) directly or indirectly comparing the effect of said test substance on the biological activities of said different target molecules;

wherein said ~~biological activities~~ target molecules are selected from the group consisting of components of a metabolic-coupled signal transduction, or a receptor-coupled signal transduction pathway. ~~one or more pathological effects, and any combination thereof.~~

62. (cancelled)

63. (currently amended) The method of claim ~~62~~ 61, wherein said different target molecules include Ras, Bcl-2 or Raf, or any combination thereof.

64. (previously presented) The method of claim 63, wherein said different target molecules include Ras.

65. (previously presented) The method of claim 63, wherein said different target molecules include Bcl-2.

66. (previously presented) The method of claim 63, wherein said different target molecules include Raf.

67. (currently amended) The method of claim 61, wherein said ~~biological activity~~ is target molecules are selected from components of a receptor-coupled signal transduction pathway.

68. (currently amended) The method of claim ~~67~~ 61, wherein said different target molecules ~~include~~ are selected from the group consisting of

- (i) receptor tyrosine kinases, serine/threonine kinases, integrin receptors, receptors of class LIF,
- (ii) oncostatin M, CNTF, gp130,
- (iii) receptor phosphatases, cytokine receptors, G-protein coupled receptors, neurokinin receptors, ~~or~~
- (iv) serotonin receptors, and
- (v) ~~or~~ any combination thereof.

69. (currently amended) The method of claim 67, wherein said different target molecules include EGF receptor, HGF receptor, HER2, KDR, neurokinin-1 receptor, neurokinin-2 receptor, or serotonin 5HT<sub>2</sub> receptor, or any combination thereof.

70. (currently amended) The method of claim 69, wherein said different target molecules include EGF receptor.

71. (currently amended) The method of claim 69, wherein said different target molecules include HGF receptor.

72. (previously presented) The method of claim 69, wherein said different target molecules include HER2.

73. (previously presented) The method of claim 69, wherein said different target molecules include KDR.

74. (currently amended) The method of claim 69, wherein said different target molecules include neurokinin-1 receptor.

75. (currently amended) The method of claim 69, wherein said different target molecules include neurokinin-2 receptor.

76. (currently amended) The method of claim 69, wherein said different target molecules include serotonin 5HT<sub>2</sub> receptor.

77. (currently amended) The method of claim 61, wherein said biological activity is an activity responsible for one or more pathological effects.

78. (currently amended) The method of claim 77, wherein said biological activity is ~~either proliferation or apoptosis or a combination thereof~~.

79. (previously presented) The method of claim 78, wherein said biological activity is proliferation.

80. (previously presented) The method of claim 78, wherein said biological activity is apoptosis.

81. (previously presented) The method of claim 61, wherein said test cells are transformed with DNA operably encoding said different target molecules.

82. (previously presented) The method of claim 81, wherein said different target molecules are receptors.

83. (previously presented) The method of claim 61, wherein said detection system is selected from a group consisting of a proliferation assay, an apoptosis assay, a reporter gene expression system, and any combination thereof.

84. (previously presented) The method of claim 83, wherein said reporter gene is selected from the group consisting of luciferase, green fluorescent protein, alkaline phosphatase,  $\beta$ -glucuronidase, chloramphenicol-acetyltransferase, and any combination thereof.

85. (previously presented) The method of claim 84, wherein said reporter gene is luciferase.

86. (previously presented) The method of claim 84, wherein said reporter gene is green fluorescent protein.

87. (previously presented) The method of claim 61, wherein said test cells are mammalian cells.

88. (previously presented) The method of claim 87, wherein said test cells are human cells.

89. (previously presented) The method of claim 61, wherein said test cells have the same genotype.

90. (currently amended) A high throughput parallel screening method of determining the pharmacological effect of a substance on the activity of the same biological target molecule contained in test cells of different types or of the same type but with a different state of differentiation or activation, comprising:

- (a) applying a defined amount of a test substance in one operation to more than one cellular substrates comprising test cells of different types or test cells of the same type but with a different state of differentiation or activation wherein said test cells contain the same biological target molecule;
- (b) measuring the effect of the substance on the biological activity of said target molecule using a detection system using different assays or assay formats for each substrate; and

(c) directly or indirectly comparing the effect of said test substance on the biological activity of said target molecule in said test cells;  
wherein said ~~biological activity~~ target molecules are selected from the group consisting of components of a metabolic-coupled signal transduction, or a receptor-coupled signal transduction pathway, ~~a pathological effect, and any combination thereof.~~

91. (cancelled)

92. (currently amended) The method of claim ~~91~~ 90, wherein said target molecule is selected from the group consisting of Ras, Bcl-2, and Raf.

93. (previously presented) The method of claim 92, wherein said target molecule is Ras.

94. (previously presented) The method of claim 92, wherein said target molecule is Bcl-2.

95. (previously presented) The method of claim 92, wherein said target molecule is Raf.

96. (currently amended) The method of claim 90, wherein said ~~biological activity~~ is target molecule is selected from components of a receptor-coupled signal transduction pathway.

97. (currently amended) The method of claim ~~96~~ 90, wherein said target molecule is selected from the group consisting of

- (i) receptor tyrosine kinases, serine/threonine kinases, integrin receptors, receptors of class LIF,
- (ii) oncostatin M, CNTF, gp130,
- (iii) receptor phosphatases, cytokine receptors, G-protein coupled receptors, neurokinin receptors, and
- (iv) serotonin receptors.

98. (currently amended) The method of claim 96, wherein said target molecule is selected from the group consisting of EGF receptor, HGF receptor, HER2, KDR, neurokinin-1 receptor, neurokinin-2 receptor, and serotonin 5HT<sub>2</sub> receptor.

99. (currently amended) The method of claim 98, wherein said target molecule is EGF receptor.

100. (currently amended) The method of claim 98, wherein said target molecule is HGF receptor.

101. (previously presented) The method of claim 98, wherein said target molecule is HER2.

102. (previously presented) The method of claim 98, wherein said target molecule is KDR.

103. (currently amended) The method of claim 98, wherein said target molecule is neurokinin-1 receptor.

104. (currently amended) The method of claim 98, wherein said target molecule is neurokinin-2 receptor.

105. (currently amended) The method of claim 98, wherein said target molecule is serotonin 5HT<sub>2</sub> receptor.

106. (currently amended) The method of claim 90, wherein said biological activity is [[a]] an activity responsible for one or more pathological effects.

107. (currently amended) The method of claim 106, wherein said ~~pathological effect~~ biological activity is ~~either~~ proliferation or apoptosis.

108. (currently amended) The method of claim 107, wherein said ~~pathological effect~~ biological activity is proliferation.

109. (currently amended) The method of claim 107, wherein said ~~pathological effect~~ biological activity is apoptosis.

110. (previously presented) The method of claim 90, wherein said target cells are transformed with DNA operably encoding said target molecule.

111. (previously presented) The method of claim 110, wherein said target molecule is a receptor.



112. (previously presented) The method of claim 90, wherein said detection system is selected from a group consisting of a proliferation assay, an apoptosis assay, a reporter gene expression system, and any combination thereof.

113. (currently amended) The method of claim 112, wherein said reporter gene is selected from the group consisting of luciferase, green fluorescent protein, alkaline phosphatase,  $\beta$ - glucuronidase, and chloramphenicol-acetyltransferase, ~~and any combination thereof.~~

114. (previously presented) The method of claim 113, wherein said reporter gene is luciferase.

115. (previously presented) The method of claim 113, wherein said reporter gene is green fluorescent protein.

116. (previously presented) The method of claim 90, wherein said test cells are mammalian cells.

117. (previously presented) The method of claim 116, wherein said test cells are human cells.

118. (previously presented) The method of claim 90, wherein said test cells are from different cell types.

119. (previously presented) The method of claim 90, wherein said test cells are of the same type, but with different states of differentiation or activation.

120. (previously presented) The method of claim 119, wherein said test cells are tumor cells and normal cells.